

Appl. No. : 10/507,277
Filed : September 10, 2004

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REMARKS

Claims 1, 3 and 4 have been amended. Claims 2, 5 and 6 have been canceled. Claims 7-13 have been withdrawn from consideration as being directed to non-elected inventions. New claim 14 has been added. Thus, Claims 1, 3, 4 and 14 are now pending in the present application. Support for the claim amendments may be found in the original claims and throughout the specification. Support for new claim 14 may be found in the specification at page 14, lines 15-18. Accordingly, the amendments do not add new matter. Reconsideration of the application in view of the foregoing amendments and following comments is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 3-4 and 6 were rejected as being indefinite based on recitation of the term "ribonucleosides" within parentheses in claims 3 and 4. Claim 6 has been canceled, thus rendering the rejection moot as it applies to this claim. Claims 3 and 4 as amended no longer recite "ribonucleosides" within parentheses.

In view of the claim amendments discussed above, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102(b)

Claim 1 was rejected as being anticipated by Yanagawa et al. (*Nucleic Acid Symposium Series* 25:113-114, 1991). In order for a claim to be anticipated by a reference, all elements recited in the claim must be found within the reference. Claim 1 as amended recites purification of 8-hydroxydeoxyguanosine from a urine sample. These features are not disclosed by Yanagawa et al. who teach purification of 8-hydroxyguanosine from Torula yeast RNA. Thus, Claim 1 cannot be anticipated by this reference.

In view of the amendments and comments presented above, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

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Rejections under 35 U.S.C. § 103(a)

Yanagawa et al.

Claim 2 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanagawa et al. The Examiner alleges that it would have been obvious to purify 8-hydroxydeoxyguanosine as presently claimed since the use of such as method using the structurally analogous 8-hydroxyguanosine is taught in the prior art, and that this reference provides motivation since good recovery of 8-hydroxyguanosine is obtained. Claim 2 has been canceled herein, and its subject matter incorporated into claim 1. Accordingly, the following remarks are directed to claim 1 (as amended) rather than to claim 2.

As discussed above, claim 1 as amended recites that the 8-hydroxydeoxyguanosine is purified from a urine sample, while Yanagawa et al. describe purification of 8-hydroxyguanosine from *Torula* yeast RNA. One of ordinary skill in the art will appreciate that since these two vastly different starting materials contain different compounds and/or contaminants, a purification method comprising anion-exchange chromatography as a first purification step for the structurally similar 8-hydroxyguanosine from *Torula* yeast RNA would not necessarily be successful in purifying 8-hydroxydeoxyguanosine from a urine sample. Because the success of anion exchange chromatography depends upon the overall charge of the composition subjected to this treatment, the results of anion exchange chromatography of a *Torula* yeast RNA preparation cannot be extrapolated to anion exchange chromatography of a urine sample. At best, it may be obvious to try to purify 8-hydroxydeoxyguanosine from a urine sample in view of Yanagawa et al., but this is not the proper standard of obviousness. There must also be a reasonable expectation that the method would be successful which is not provided by Yanagawa et al. One of ordinary skill in the art would have no idea whether a technique used for purifying a ribonucleoside from a yeast RNA preparation could be successfully used to purify the corresponding deoxyribonucleoside from a urine sample. Thus, the reasonable expectation of success required for a *prima facie* case of obviousness is entirely absent.

Moreover, amended claim 1 recites that the purification step is conducted using an anion-exchange resin having a particle diameter of 7 to 12 μm which facilitates isolation of 8-hydroxydeoxyguanosine in highly purified form. This is not taught or even remotely suggested

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by Yanagawa et al. who disclose resin AG1-X2 (Bio-Rad Laboratories) which has a particle diameter of 75-180 μm . Based on the Examiner's acknowledged "good recovery of the analogous 8-hydroxyguanosine" by Yanagawa et al., one of ordinary skill in the art would not have been motivated to use an anion exchanger having a particle size an order of magnitude smaller than that used by Yanagawa et al. Based on the successful results obtained by Yanagawa et al. using the resin having a particle diameter of 75-180 μm , there would simply be no suggestion or motivation to decrease the particle diameter to 7 to 12 μm as presently claimed, because this could significantly compromise the results of the anion exchange chromatography obtained by Yanagawa et al.. Thus, Applicant submits that claim 1, and all claims dependent thereon, is not obvious in view of Yanagawa et al.

Park et al.

Claim 3 was rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al. (*Carcinogenesis* 10:827-832, 1989). Claim 3, which depends on claim 1, recites that the 8-hydroxydeoxyguanosine ribonucleoside (8-OH-rGuo) is previously added to the sample as an internal standard marker for 8-OH-dG. Claim 1 was not rejected as obvious in view of Park because this reference does not suggest a purification method for 8-hydroxydeoxyguanosine (8-OH-dG) contained in a urine sample, comprising a first purification step for purifying the 8-OH-dG contained in the urine sample by anion-exchange chromatography using a resin having a particle diameter of 7 to 12 μm , nor does this reference provide motivation to arrive at the claimed method. Because claim 1 is not obvious over this reference, then any claim dependent thereon is necessarily not obvious in view of this reference.

In addition, Park et al. neither discloses nor suggests the relationship between the elution position of 8-OH-dG and that of 8-OH-rGuo in anion exchange chromatography. Without this disclosure or suggestion, one skilled in the art would not have been motivated to add 8-OH-rGuo to the sample so as to effectively purify 8-OG-dG. Thus, Claim 3 is not obvious over Park et al.

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Yanagawa et al. in combination with with Park et al.

Claim 4 was rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa et al. in combination with Park et al. Claim 4 depends on claim 1. As discussed above, claim 1 is not obvious over either of these references alone. Thus, claim 4 is also not obvious in view of either of these references taken alone. The combination of references does not cure the defects in the teaching of either individual reference since the following claim elements are neither taught nor suggested by either reference: purification from a urine sample and a resin having a particle diameter of 7 to 12 μm . Thus, claim 4 is not obvious in view of this combination of references.

Yanagawa et al. in combination with Park et al. and Loft et al.

Claims 5 and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa et al. in combination with Park et al. and Loft et al. (*J. Toxicol. Environmental Health* 40:391-404, 1993). Claims 5 and 6 have been canceled herein, and the feature recited therein, namely purification from a urine sample, has been incorporated into claim 1. Thus, the rejection will be addressed as it applies to amended claim 1.

As discussed above, Yanagawa et al. combined with Park et al. does not render claim 1 obvious. Although Loft et al. disclose analysis and separation of 8-hydroxydeoxyguanosine in urine using HPLC, Loft does not disclose (or suggest) that such separation may be achieved using anion-exchange chromatography, or a resin having the particle size recited in claim 1. Thus, Loft et al. does not cure the defects in the teachings of Yanagawa et al. and Park et al., namely anion-exchange chromatography of a urine sample, and an anion-exchange resin having a particle diameter of 7 to 12 μm . Thus, claim 1 is not obvious in view of this combination of references.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a).

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CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited. If any minor issues remain which could be resolved by telephone, the Examiner is invited to contact the undersigned at the number provided below.

Respectfully submitted,

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